REMARKS

1. Status of claims

Claims 7-10 and 12-33 are pending and under consideration. Claims 1-6 and 35 have been withdrawn from consideration, and claims 11, 34, and 36-40 have been canceled.

2. Support for amendment

The above amendment finds support in the specification at p. 19, lines 19-21. No new matter has been added by this amendment.

3. Objection to the specification

The Examiner objected to the amendment to the specification filed on December 19, 2006 under 35 U.S.C. § 132(a) as allegedly containing new matter. Applicants submit the amendment to the specification is supported by the application as originally filed (MPEP 2163.07). Specifically, Example 3 teaches that gene sequences were amplified by PCR and cloned into the pSTBlue-1 plasmid (p. 26, lines 11-12), and Example 4 teaches that the resultant plasmids were designated pSTB XXX-Y, wherein XXX is the name of the gene amplified in Example 3 and Y indicates whether the gene is in the sense or the antisense orientation (p. 28, lines 18-21). The person of ordinary skill in the art would understand from the discussion at p. 27, lines 22-24 that the tables at p. 27, line 26 to p. 28, line 1 report the plasmid from Example 3 used as the source of the gene, the pYX plasmid into which the gene is cloned, the restriction enzyme(s) used to cut the gene from the pSTB XXX-Y plasmid and to cut the pYX plasmid to allow cloning of the gene therein, and would conclude the pZ XXX name refers to the variant of

the pYX plasmid produced by insertion of the cloned gene. Therefore, the objected matter is a rephrasing of matter already included within the specification, and therefore is not new matter.

The Examiner also objected to the amendment at p. 29, lines 21-24, as adding new matter. By the above amendment, the added information has been removed from the passage.

4. Claim rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 7-10 and 12-33 for allegedly being indefinite for reciting "L-gulono-1,4-lactone oxidase (RGLO)," on the ground that the specification defines "L-gulono-1,4-lactone oxidase" as any enzyme that catalyzes the oxidation of L-gulono-1,4,-lactone to L-xylohexulonolactone and "RGLO" as the L-gulono-1,4-lactone oxidase from *R. norvegicus*. By the above amendment, the claims recite "L-gulono-1,4-lactone oxidase." Applicants therefore request this rejection of claims 7-10 and 12-33 be withdrawn.

5. Claim rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 7-10 and 12-33 for allegedly failing to comply with the written description requirement. Specifically, the Examiner alleged that the specification did not reasonably convey to the skilled artisan that the inventors had possession of the claimed invention, specifically relating to methods of generating ascorbic acid by use of yeast transformed with a coding region encoding D-arabinose dehydrogenase (ARA), D-arabinono-1,4-lactone oxidase (ALO), or L-gulono-1,4-lactone oxidase; including such coding regions having or encoding an enzyme having at least about 70% similarity or identity to various sequences (claims 12-14), or coding regions isolated from various species (claim 20). Applicants traverse this rejection.

The written description requirement set forth in 35 U.S.C. §112, first paragraph implements the principle that a patent must describe the technology that is sought to be patented. The written description requirement also conveys that an applicant has invented the subject matter which he claims.

In *Capon v. Eshhar*, 76 USPQ2d 1078 (Fed. Cir. 2005), the United States Court of Appeals for the Federal Circuit addressed the written description requirement and also touched on its relationship to the enablement requirement and issues of claim scope. The present specification, in light of the holdings in *Capon v. Eshhar*, supports Applicants' contention that the claims comply with the written description requirement.

It is clear that the terms D-arabinose dehydrogenase (ARA), D-arabinono-1,4-lactone oxidase (ALO), and L-gulono-1,4-lactone oxidase each had a plain and precise meaning well-known in the art as of the priority date of the present application. Specifically, "D-arabinose dehydrogenase (ARA)" refers to an enzyme that catalyzes the conversion of D-arabinose to D-arabinono-1,4-lactone; "D-arabinono-1,4-lactone oxidase (ALO)" refers to an enzyme that catalyzes the conversion of D-arabinono-1,4-lactone to erythroascorbic acid; and "L-gulono-1,4-lactone oxidase" refers to an enzyme that catalyzes the conversion of L-gulono-1,4-lactone to ascorbic acid (Enzyme Commission (EC) 1.1.3.8, p. 7, line 14).

As will be clear, claim 7 encompasses any method of generating ascorbic acid by use of yeast transformed with a coding region encoding ARA, ALO, or L-gulono-1,4-lactone oxidase. Claims 12-14 recite not ARA, ALO, or L-gulono-1,4-lactone oxidase *per se* but ARAs, ALOs, or L-gulono-1,4-lactone oxidases having at least about 70% similarity with SEQ ID NO:20, 5 or 7, or 9, respectively (claim 12), having at least about 70% identity with SEQ ID NO: 20, 5 or 7, or 9, respectively (claim 13), or being encoded by a coding region having at least about 70%

identity with SEQ ID NO:21, 6 or 8, or 10, respectively (claim 14). Claims 20-26 recite not ARA, ALO, or L-gulono-1,4-lactone oxidase *per se* but ARAs, ALOs, or L-gulono-1,4-lactone oxidases derived from *Arabidopsis thaliana*, *Saccharomyces cerevisiae*, or *Rattus norvegicus*.

On their face, the teachings of the specification relating to the recited ARAs, ALOs, or L-gulono-1,4-lactone oxidases comply with the purposes of the written description requirement; the public receives meaningful disclosure of what Applicants invented, as the genera of recited ARAs, ALOs, or L-gulono-1,4-lactone oxidases have clear metes and bounds and clear instruction for practicing the invention upon its future entry into the public domain, and also to clearly convey that Applicants invented what they claim.

It is true that Applicants only enumerated ARAs, ALOs, or L-gulono-1,4-lactone oxidases having SEQ ID NO:20, 5 or 7, or 9, respectively or encoded by SEQ ID NO: 21, 6 or 8, or 10, respectively. Even so, ARAs, ALOs, or L-gulono-1,4-lactone oxidases possess sufficient written description, for several reasons. First, as will be apparent to the skilled artisan, there are a vast number of ARAs, ALOs, or L-gulono-1,4-lactone oxidases. The impossibility of listing every such sequence is apparent. However, listing every such sequence is not required; as the Court held in *Capon v. Eshhar*, there is no *per se* rule that a sequence listing must be presented for every biological sequence claimed in a patent application. 76 USPQ2d at 1084-1085. Also as held in *Capon v. Eshhar*, the written description requirement "does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." *Id.*, at 1085. Also, any ARA, ALO, or L-gulono-1,4-lactone oxidase, regardless of its amino acid sequence, would be operable in the claimed methods.

Regarding claims 12-14, the claims are plainly not drawn to methods using any member of the set of all proteins having at least about 70% similarity or at least about 70% identity to SEQ ID NO:20, 5, 7, or 9 or being encoded by a coding region having at least about 70% identity to SEQ ID NO:21, 6, 8, or 10. Rather, claims 12-14 are plainly drawn methods using ARAs, ALOs, or L-gulono-1,4-lactone oxidases, wherein the ARAs, ALOs, or L-gulono-1,4-lactone oxidases have the recited levels of similarity or identity. The Examiner's citation of a guinea pig protein that has 79% amino acid homology to rat L-gulono-1,4-lactone oxidase but does not have L-gulono-1,4-lactone oxidase activity (Detailed Action, p. 9) has no bearing on claims 12-14, which recite a protein that *both* has L-gulono-1,4-lactone oxidase activity *and* 70% identity with SEQ ID NO:9.

In addition, the Court in *Capon v. Eshhar* addressed what is needed to support generic claims and held "It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention" (at 1085). Applicants discuss the generation of recombinant yeast at p. 11, line 26 to p. 17, line 2, and provide specific examples of coding region amplification, transformation into yeast, ascorbic acid production, and assay of same, at p. 23, line 30 to p. 31, line 5. Applicants cite 26 references discussing various aspects of the art and also cite Sambrook *et al.*, *Molecular Genetics: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, which is one of the best-known references for laboratory techniques, including techniques which can be used to prepare ARA, ALO, or L-gulono-1,4-lactone oxidase proteins. On reading the teachings of the specification in light of the state of the art, the skilled artisan would consider the claims to have support according to the holdings of *Capon v. Eshhar*.

Another case which discusses written description is *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). However, *Lilly* is not applicable to the facts of the present case. The *Lilly* court held that the disclosure of a rat-insulin encoding cDNA did not provide sufficient written description for the genera of "mammalian insulin cDNA" or "vertebrate insulin cDNA." These facts are distinct over the facts of the present case in a number of ways. First, as is known to a person of ordinary skill in the art, a cDNA is a nucleic acid molecule derived from (actual or conceptual) reverse transcription of an mRNA molecule encoding a particular protein. The term "cDNA" therefore requires knowledge or discovery of the sequence of the mRNA molecule encoding the particular protein. Given the degeneracy of the genetic code, many possible mRNA sequences could encode a particular protein sequence, and therefore the sequence of a cDNA can only be determined or predicted after possession of its corresponding mRNA sequence. For these reasons, the *Lilly* court held that a description of the amino acid sequence of human insulin did not provide written description of the cDNA sequence encoding human insulin, because an amino acid sequence cannot be used to derive a cDNA sequence. In contrast, in the present application, the terms ARA, ALO, or L-gulono-1,4-lactone oxidase refer to enzymes having particular functions (*i.e.*, the conversion of D-arabinose to D-arabinono-1,4-lactone, the conversion of D-arabinono-1,4-lactone to erythroascorbic acid, or the conversion of L-gulono-1,4-lactone to ascorbic acid, respectively) and is independent of any actual or conceptual derivation of that function from a particular protein or nucleic acid molecule.

Even if *Lilly* could properly be applied to the facts of the present case, the claims would be found to have sufficient written description in light of *Lilly* and other cases cited at MPEP 2603. MPEP 2603 holds "when there is substantial variation within the genus, one must describe

a sufficient variety of species to reflect the variation within the genus." No substantial variation exists within the genera of ARAs, ALOs, or L-gulono-1,4-lactone oxidases enzymes. No substantial variation exists in the genera of enzymes able to catalyze conversion of the conversion of D-arabinose to D-arabinono-1,4-lactone, the conversion of D-arabinono-1,4-lactone to erythroascorbic acid, or the conversion of L-gulono-1,4-lactone to ascorbic acid, *i.e.*, the genera of ARAs, ALOs, or L-gulono-1,4-lactone oxidases, respectively. Any variation between any two or more enzymes within each of the genera would be in the realm of reaction kinetics, *e.g.*, how fast the conversion would take place or what the equilibrium levels of products or reactants in the absence of addition or removal of either or both compounds would be; such variation would not be "substantial." Also, no unpredictability exists in the results obtained from species other than those specifically enumerated. Any members of the genera of ARAs, ALOs, or L-gulono-1,4-lactone oxidases enzymes would predictably have the ability to catalyze conversion of D-arabinose to D-arabinono-1,4-lactone, the conversion of D-arabinono-1,4-lactone to erythroascorbic acid, or the conversion of L-gulono-1,4-lactone to ascorbic acid, respectively.

Particularly considering claims 12-14, if no substantial variation exists within the genera of ARAs, ALOs, or L-gulono-1,4-lactone oxidases, it follows that no substantial variation can exist within the subgenera of ARAs, ALOs, or L-gulono-1,4-lactone oxidases enzymes having at least about 70% similarity or at least about 70% identity with SEQ ID NO:20, 5 or 7, or 9, respectively, or coding regions having at least about 70% identity with SEQ ID NO:21, 6, 8, or 10.

The Examiner also made a statement on which Applicants wish to comment. At Detailed Action, p. 8, he wrote, "It is not even clear from the specification what the differences between

the two disclosed ALO sequences are." The sequences are both given in the specification at pp. 42-46, and their differences can be readily determined. Specifically, they differ at position 417, alanine in SEQ ID NO:5 and proline in SEQ ID NO:7.

For at least the foregoing reasons, Applicants request this rejection of claims 7-10 and 12-33 be withdrawn.

The Examiner also rejected claim 10 as failing to comply with the enablement requirement, specifically, for failing to properly provide to the public information concerning strains deposited under the Budapest Treaty and removal of restrictions on access thereto upon grant of the patent. The Examiner also stated that Applicants had failed to provide deposit information for *K. lactis* PM6-7A.

Applicants enclose herewith a Declaration by Chi-Li Liu regarding the strains deposited on behalf of the present Applicants. *K. lactis* PM6-7A was not deposited because it is known to the public and originally constructed by other workers, specifically, Wésoloswki-Louvel's group, as indicated in the specification at p. 28, lines 3-5. Applicants submit the basis for this rejection has been removed.

6. Conclusion

Applicants submit all pending claims are in condition for allowance. The Examiner is invited to contact the undersigned patent agent at (713) 934-4065 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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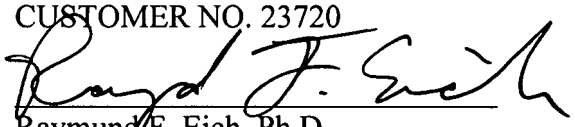

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